APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO.
08/977,862	11/25/97	LAWRENCE	

G   GH-30170
EXAMINER

HM21/0928

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ART UNIT	PAPER NUMBER
1645	6

DATE MAILED:

09/28/98

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☐ Responsive to communication(s) filed on _____

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire ___**3**___ month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☑ Claim(s) ___1-27___ is/are pending in the application.

Of the above, claim(s) ___6 - 22 + 25 - 27___ is/are withdrawn from consideration.

☑ Claim(s) ___24___ is/are allowed.

☑ Claim(s) ___1-5 + 23___ is/are rejected.

☐ Claim(s) _____ is/are objected to.

☑ Claim(s) ___1 - 27___ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
☐ The specification is objected to by the Examiner.
☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☑ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☑ All ☐ Some* ☐ None   of the CERTIFIED copies of the priority documents have been

☑ received.
☐ received in Application No. (Series Code/Serial Number) _____.
☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of Reference Cited, PTO-892
☑ Information Disclosure Statement(s), PTO-1449, Paper No(s). ___4___
☐ Interview Summary, PTO-413
☐ Notice of Draftsperson's Patent Drawing Review, PTO-948
☐ Notice of Informal Patent Application, PTO-152

--SEE OFFICE ACTION ON THE FOLLOWING PAGES--

Part III   DETAILED ACTION

1.   Restriction to one of the following inventions is required under 35 U.S.C. 121:

Group I. Claims 1-5 and 23-24, drawn to polypeptides, classified in class 530, subclass 350, for example.

Group II. Claims 6-16 and 26-27, drawn to polynucleotides, classified in class 536, subclass 23.5, for example.

Group III. Claim 17, drawn to an antibody, classified in class 530, subclass 387.1, for example.

Group IV. Claim 18, drawn to a method of treatment by administering an agonist, classified in class 514, subclass 2, for example.

Group V. Claim 18, drawn to a method of treatment by administering a polynucleotide, classified in class 514, subclass 44, for example.

Group VI. Claim 19, drawn to a method of treatment by administering an antagonist or polypeptide antagonist, classified in class 514, subclass 2, for example.

Group VII. Claim 19, drawn to a method of treatment by administering an antisense polynucleotide, classified in class 514, subclass 44, for example.

Group VIII. Claim 20, drawn to a method of diagnosis using nucleotide sequence, classified in class 435, subclass 6, for example.

Group IX. Claim 20, drawn to a method of diagnosis using polypeptide expression, classified in class 435, subclass 7.2, for example..

Group X. Claim 21, drawn to an agonist, classified in class 530, subclass 350, for example.

Group XI. Claim 22, drawn to an antagonist, classified in class 530, subclass 387.1, for example.

2.   The inventions are distinct, each from the other because of the following reasons:

Although there are no provisions under the section for "Relationship of Inventions" in MPEP 806.05 for "inventive groups that are directed to different products; restriction is deemed to be proper because these products appear to constitute patentably distinct inventions for the following reasons:

Groups I-III and X-XI are directed to products that are distinct physically, structurally, and functionally, and are therefore patentably distinct, each group from the other, and are not required one for the other. Each group comprises a separate and distinct nucleic acid, polypeptide, agonist, antagonist, or antibody. The nucleic acid encoding a particular polypeptide does not have to be used to make that polypeptide, but can be used as a probe. The polypeptide receptor(s) can be used other than to make a specific antibody against it, but can be used therapeutically. The antibodies can be used other than to make the receptor(s) by isolation and purification from a natural source, but can be used to detect the receptor(s) in an assay or used therapeutically. The agonist may be used therapeutically or labeled for diagnostic or screening purposes. The antagonist may be used therapeutically or labeled for diagnostic or screening purposes.

3.   Groups I, II, III, X, and XI and Groups IV (for X), V (for II), VI (for III and XI), VIII (for II), and IX (for III, X, and XI) are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the nucleic acid encoding a particular polypeptide does not have to be used therapeutically but can also be used diagnostically as a probe. The polypeptide receptor(s) can be used other than therapeutically, such as for the production of specific antibodies. The antibodies can be used as antagonists or to make the receptor(s) by isolation and purification from a natural source. The agonist may be used therapeutically or labeled for diagnostic or screening purposes. The antagonist may be used therapeutically or labeled for diagnostic or screening purposes.

4.   Although there are no provisions under the section for "Relationship of Inventions" in MPEP 806.05 for "inventive groups that are directed to <u>different</u> methods; restriction is deemed to be proper because these methods appear to constitute patentably distinct inventions for the following reasons:

Groups IV-IX are directed to methods that comprise distinct process steps and use distinct products that are different physically, structurally, and functionally, and are therefore patentably distinct, each group from the other, and are not required one for the other. Each group comprises methods using a separate and distinct polypeptide, agonist, antagonist, antibody and/or encoding nucleic acid or antisense nucleic acid.

5.   Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their separate classifications and because the literature searches required for the inventions are not co-extensive and therefore references that would anticipate one invention would not necessarily anticipate or even make obvious the other invention, a search burden exists, and restriction for examination purposes as indicated is proper. Furthermore, there are different issues for the search and examination of each, which would also be unduly burdensome.

Applicant is advised that the response to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed.

During a telephone conversation with Robert Anderson on 8/20/98 a provisional election was made with traverse to prosecute the invention of Group I, claims 1-5 and 23-24. Affirmation of this election must be made by applicant in replying to this Office action. Claims 6-22 and 24-27 withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

6.   Claim 23 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a fragment of SEQ ID NO:6, does not reasonably provide enablement for a GDNF alpha 3 receptor "characterised" by SEQ ID NO:6. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims. SEQ ID NO:6 is a partial polypeptide sequence for a GDNF alpha 3 receptor that is less than half (172 amino acids) the sequence length of the full-length GDNF alpha 3 receptor disclosed (SEQ ID NO:2, 400 amino

acids). The disclosure does not place a GDNF alpha 3 receptor "characterised" by SEQ ID NO:6

into the hands of the skilled artisan for the following reasons. SEQ ID NO:6 has support in the

foreign priority documents as far back as 11/27/96. SEQ ID NO:4 was disclosed in the priority

documents as of 5/9/97. The actual filing date of the instant Application is 11/25/97 and SEQ ID

NO:2 is taught at this time. However, no further enabling support for a GDNF alpha 3 receptor

"characterised" by SEQ ID NO:6 is disclosed in the specification and there is insufficient

guidance, examples, or description of such a receptor that the skilled artisan could make or use

such a receptor with a reasonable expectation of success because the term "receptor" is known in

the art to mean a binding and biological activity function. No working examples of such a

functional receptor are disclosed, and the complete sequence of such a functional receptor cannot

be predicted from the partial amino acid sequence provided even though the average skill in the

molecular biology arts is high. Given that there are highly similar receptors present in their

natural state (exemplified by SEQ ID NO:2), it would require undue experimentation for the

skilled artisan to make the receptor as claimed because of the degree of interference provided by

competing similar receptor subtypes and the apparent difficulty in isolating this particular subtype

as Applicant has not disclosed the full sequence a year after the initial discovery of the partial

sequence, but has been able to isolate another closely related sequence.

7.   Claims 1-5 and 23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite

for failing to particularly point out and distinctly claim the subject matter which applicant regards

as the invention. The specification on page 18, line 26 to page 19, line 2, describes several

methods to compute sequence identity. However, the claims are indefinite because it is not clear

which method and what parameters within that method are being used, so the metes and bounds of the claims are indeterminate because different methods will produce variable sequence identity percentages.

Claim 5 is indefinite because a polypeptide is not a sequence, but a polypeptide can have the amino acid sequence of SEQ ID NO:2 or SEQ ID NO:4 (compare claim 5 with claim 24).

Claim 23 is indefinite because it is unclear how a polypeptide is "characterised" by an amino acid sequence. A polypeptide can consist of or comprise a certain sequence, but "characterised" is vague and indefinite as to its exact relationship to the sequence.

8.   The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9.   Claim 23 is rejected under 35 U.S.C. 102(b) as being anticipated by Jing et al. ("Jing"). Jing discloses retinal cell cultures that contain an isoform of GDNF alpha that are processed in the proteolytic enzyme papain (page 1120). Jing's polypeptide contains fragments of SEQ ID NO:6 (see attached sequence listing). Jing's process would inherently produce fragments that would match partial sequences of SEQ ID NO:6. It is also noted that Jing supplements his culture media with glutamine (page 1121). Glutamine is a single amino acid fragment of the claimed invention.

10.   Claim 24 is in condition for allowance.

11.   Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephen Gucker whose telephone number is (703) 308-6571. The examiner can normally be reached on Monday to Thursday from 0730 to 1800.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Paula Hutzell, Ph.D., can be reached on (703) 308-4310. The fax phone number for this Group is currently (703) 308-4242, but Applicant should confirm this by phoning the Examiner before faxing.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Stephen Gucker

September 24, 1998

PAULA K. HUTZELL
SUPERVISORY PATENT EXAMINER

RESULT 5

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ID   GDNR_MOUSE      STANDARD;      PRT;   468 AA.
AC   P97785;
DT   01-NOV-1997 (REL. 35, CREATED)
DT   01-NOV-1997 (REL. 35, LAST SEQUENCE UPDATE)
DT   01-NOV-1997 (REL. 35, LAST ANNOTATION UPDATE)
DE   GDNF RECEPTOR ALPHA PRECURSOR (GDNFR-ALPHA) (TGF-BETA RELATED
DE   NEUROTROPHIC FACTOR RECEPTOR 1).
GN   GDNFRA OR TRNR1.
OS   MUS MUSCULUS (MOUSE).
OC   EUKARYOTA; METAZOA; CHORDATA; VERTEBRATA; TETRAPODA; MAMMALIA;
OC   EUTHERIA; RODENTIA.
RN   [1]
RP   SEQUENCE FROM N.A.
RC   TISSUE=DORSAL ROOT GANGLION;
RA   WATABE K.;
RL   SUBMITTED (FEB-1997) TO EMBL/GENBANK/DDBJ DATA BANKS.
CC   -!- FUNCTION: RECEPTOR FOR GDNF. MEDIATES THE GDNF-INDUCED
CC       AUTOPHOSPHORYLATION AND ACTIVATION OF THE RET RECEPTOR (BY
CC       SIMILARITY).
CC   -!- SUBUNIT: 2 MOLECULES OF GDNFR-ALPHA ARE THOUGHT TO FORM A COMPLEX
CC       WITH THE DISULFIDE-LINKED GDNF DIMER AND WITH 2 MOLECULES OF RET
CC       (BY SIMILARITY).
CC   -!- SUBCELLULAR LOCATION: ATTACHED TO THE MEMBRANE BY A GPI-ANCHOR (BY
CC       SIMILARITY).
CC   -!- SIMILARITY: BELONGS TO THE GDNFR FAMILY.
DR   EMBL; AB000800; G1816442; -.
KW   RECEPTOR; GLYCOPROTEIN; GPI-ANCHOR; MEMBRANE; SIGNAL.
FT   SIGNAL        1     24       POTENTIAL.
FT   CHAIN        25      ?       GDNF RECEPTOR ALPHA.
FT   PROPEP        ?    468       HYDROPHOBIC, REMOVED DURING MATURATION
FT                                (POTENTIAL).
FT   DOMAIN      362    369       POLY-THR.
FT   CARBOHYD     59     59       POTENTIAL.
FT   CARBOHYD    347    347       POTENTIAL.
FT   CARBOHYD    406    406       POTENTIAL.
SQ   SEQUENCE   468 AA;  51782 MW;  6C64C182 CRC32;
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Query Match             28.2%;   Score 369;  DB 1;  Length 468;
Best Local Similarity   46.7%;   Pred. No. 1.50e-62;
Matches    57;   Conservative   19;   Mismatches   43;   Indels   3;   Gaps   3;

Qy  223  ERRQTIYPVCSYEERERPNCLNLQDSCKTNYICRSRLADFFTNCQPESRSVSNCLKENY  282
             ||||||| |  |||   ||| ::|| | ||| || :| | |  | | ::| |
Db    1  ERRRNTIAPNCALPPVA-PNCLELRRLCFSDPLCRSRLVDFQTHCHPMDI-LGTCATEQ-  57

Qy  283  ADCLLAYSGLIGTVMTPNYIDSSSLSVAPWCDCSNSGNDLEDCLKFLNFFKDNTCLKNAI  342
             : ||||||||||||| ||||:: |||::: |||  |   |||  | ||  :||
Db   58  SRCLRAYLGLIGTAMTPNFVSNVNTSVALSCTCRGSGNLQEECEMLEGFFSHNPCLTEAI  117
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Qy  118 AA 119
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RESULT 6

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ID   GDNR_CHICK      STANDARD;      PRT;   469 AA.
AC   O13156;
DT   01-NOV-1997 (REL. 35, CREATED)
DT   01-NOV-1997 (REL. 35, LAST SEQUENCE UPDATE)
DT   01-NOV-1997 (REL. 35, LAST ANNOTATION UPDATE)
DE   GDNF RECEPTOR ALPHA PRECURSOR (GDNFR-ALPHA) (TGF-BETA RELATED
DE   NEUROTROPHIC FACTOR RECEPTOR 1).
GN   GDNFRA.
OS   GALLUS GALLUS (CHICKEN).
OC   EUKARYOTA; METAZOA; CHORDATA; VERTEBRATA; TETRAPODA; AVES; NEOGNATHAE;
OC   GALLIFORMES.
RN   [1]
RP   SEQUENCE FROM N.A.
RA   BUJ-BELLO A., ADU J., PINON L.G., HORTON A., THOMPSON J.,
RA   ROSENTHAL A., CHINCHETRU M., BUCHMAN V.L., DAVIES A.M.;
RL   NATURE 387:721-724(1997).
CC   -!- FUNCTION: RECEPTOR FOR GDNF. MEDIATES THE GDNF-INDUCED
CC       AUTOPHOSPHORYLATION AND ACTIVATION OF THE RET RECEPTOR (BY
CC       SIMILARITY).
CC   -!- SUBUNIT: 2 MOLECULES OF GDNFR-ALPHA ARE THOUGHT TO FORM A COMPLEX
CC       WITH THE DISULFIDE-LINKED GDNF DIMER AND WITH 2 MOLECULES OF RET
CC       (BY SIMILARITY).
CC   -!- SUBCELLULAR LOCATION: ATTACHED TO THE MEMBRANE BY A GPI-ANCHOR (BY
CC       SIMILARITY).
CC   -!- SIMILARITY: BELONGS TO THE GDNFR FAMILY.
DR   EMBL; U90541; G2213803; -.
KW   RECEPTOR; GLYCOPROTEIN; GPI-ANCHOR; MEMBRANE; SIGNAL.
FT   SIGNAL        1     27       POTENTIAL.
FT   CHAIN        28      ?       GDNF RECEPTOR ALPHA.
FT   PROPEP        ?    469       HYDROPHOBIC, REMOVED DURING MATURATION
FT                                (POTENTIAL).
FT   DOMAIN      361    368       POLY-THR.
FT   CARBOHYD     62     62       POTENTIAL.
FT   CARBOHYD    163    163       POTENTIAL.
FT   CARBOHYD    346    346       POTENTIAL.
FT   CARBOHYD    405    405       POTENTIAL.
SQ   SEQUENCE   469 AA;  52043 MW;  CBD241C9 CRC32;
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Query Match             28.2%;   Score 369;  DB 1;  Length 469;
Best Local Similarity   46.7%;   Pred. No. 1.50e-62;
Matches    57;   Conservative   19;   Mismatches   43;   Indels   3;   Gaps   3;

Qy  222  ERRQTIYPVCSYEDREKPNCLLNLQESCKRNYICRSRLADFFTNCQPESRSVSSCLKENY  281
             ||||||| |  |||   ||| ::|| | ||| || :| | |  | | ::| |
Db    1  ERRRNTIAPNCALPPVA-PNCLELRRLCFSDPLCRSRLVDFQTHCHPMDI-LGTCATEQ-  57

Qy  282  ADCLLAYSGLIGTVMTPNYIDSSSLSVAPWCDCSNSGNDIDECRKFLNFFQDNTCLKNAI  341
             : ||||||||||||| ||||:: |||::: |||  |   |||  | ||  :||
Db   58  SRCLRAYLGLIGTAMTPNFVSNVNTSVALSCTCRGSGNLQEECEMLEGFFSHNPCLTEAI  117
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Qy  118 AA 119
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RESULT 7

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ID   GDNR_HUMAN      STANDARD;      PRT;   464 AA.
AC   P56159;
DT   01-NOV-1997 (REL. 35, CREATED)
DT   01-NOV-1997 (REL. 35, LAST SEQUENCE UPDATE)
DT   01-NOV-1997 (REL. 35, LAST ANNOTATION UPDATE)
DE   GDNF RECEPTOR ALPHA PRECURSOR (GDNFR-ALPHA) (TGF-BETA RELATED
DE   NEUROTROPHIC FACTOR RECEPTOR 1).
GN   GDNFRA OR TRNR1.
OS   HOMO SAPIENS (HUMAN).
OC   EUKARYOTA; METAZOA; CHORDATA; VERTEBRATA; TETRAPODA; MAMMALIA;
OC   EUTHERIA; PRIMATES.
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Qy  118 AA 119
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